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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,478	11/17/2000	Beth Anne Allison	2196/1E500	7552

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EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	21

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/715,478	ALLISON ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response filed February 10, 2003 have been entered.

In view of the applicant's remarks of teaching away in Vincent et al. was found persuasive. The outstanding rejections under 35 USC 103(a) is withdrawn in view of applicant's remarks. Since there is contradicting effects on intimal hyperplasia by using BPD-MA photodynamic therapy, no reasonably expectation is present in the cited prior art. Therefore, the herein claimed method of treating, reducing, and inhibiting restenosis or intimal hyperplasia employing green porphyrin, such as BPD-MA and A-EA6 is considered free of prior art.

Upon reconsideration, the rejection under 35 USC 112, second paragraph is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 and 12-19 of U.S. Patent No. 09/716,022 (herein after referred as '022). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The conflicting claims in '022 recited the method of treating blood vessel grafts, including arteries and veins graft with the instant photodynamic therapeutic agents along with irradiation to prevent, treat, reduce or inhibit restenosis or intimal hyperplasia.

The claims in '022 do not teach that 1) the specific dosing range ($0.25 - 25 J/cm^2$) as recited in the instant claims; and 2) the instant claims employ the photodynamic agents within a specific time of angioplasty procedure.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the specific herein claimed dosage regimen (i.e., the specific dosing range and timing of photodynamic therapy).

One of ordinary skill in the art would have been motivated to employ the specific herein claimed dosage regimen because optimization of dosing regimen is obvious as being within the skilled artisan. Furthermore, angioplasty is a common procedure employed to treat restenosis or intimal hyperplasia in artery graft, which is commonly used in coronary bypass graft procedure.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

The claims herein are very broad. As Applicant's points out in the reply filed February 10, 2003, page 4, second paragraph, the term prevent would encompass every degree of prevention, which includes absolute prevention. In the instant case, the

specification fails to provide guidance as to how one skilled in the art would go about preventing restenosis or IH or how the arteries could be kept from being susceptible to these pathogenic changes ever again. Nor is there any guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed method in preventing restenosis or IH. It is well known in the art, as evidenced by the articles provided through the IDS received October 1, 2001 and March 19, 2002, that absolute prevention of restenosis or IH is not likely. The art is focus on how to reduce the degree of or treat the already existed restenosis or IH. It is unclear how one of skilled artisan would be able to absolutely prevent restenosis or IH. Therefore, the quantity of experimentation would be enormously large for determining an embodiment to achieve the envisioned absolute preventive effect. Moreover, it is highly unlikely and unpredictable, if not nearly impossible, that after applying the herein claimed method once, there will not be any restenosis or IH occur ever again (i.e., absolute prevention) in the site of application. Examiner notes that Vincent et al., reference of record in the previous Office action, page 76, second paragraph, teaches that "intimal damage by virtually any means may induce a profliferative response." Furthermore, there is no working example disclosed in the specification in regard to the prevention of restenosis or IH. The burden of enabling the prevention of restenosis or intimal hyperplasia (IH) (i.e. the need for additional testing) is greater than that of enabling a treatment for restenosis or IH. The specification fails to enable one of ordinary skill in the art to practice and use the methods of instant claims 1-10. Absent such information or

guidance, one of skilled artisan would be required to perform undue experimentation in order to practice the herein claimed method of preventing restenosis or IH.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vincent'362 (US Patent 5,422,362, reference of record) in view Gonschlor et al. (Photochemistry and Photobiology, 1996; 64(5):758-763 from the IDS received October 5, 2001) and Harrison (Harrison's Principle of Internal Medicine, 13h ed., 1994, page 986, published by McGraw Hill).

Vincent'362 teaches Sobeh using Photofrin II, also known as porfimer sodium, in the concentration of 2μg/ml, to treat restenosis with light energy of greater than 3 J/cm^2. Such treatment results in the destruction of over 80% of smooth muscle cells (See col.

2, line 40-57). Vincent'362 teaches Dartsch using Photofrin II to markedly reduce plaque-derived smooth muscle cells without totally destroy the normal viable cells (See col. 2, line 12-39). Vincent'362 teaches the energy used in the Dartsch's experiment as $1.2J/cm^2$ (see col. 2, line 34). Vincent'362 teaches Eton et al. using Photofrin II in rabbit model underwent standardized intimal injury to both common carotid arteries and balloon catheter (See col. 3, lines 6-22). Vincent'362 also teaches Eton et al. reported that Photofrin II and irradiation significantly improve the ratios of the area of IH to that enclosed by the internal elastic lamina (See col. 3, lines 15-22).

Vincent'362 does not expressly teach the injury is accompanied by angioplasty procedure using a stent. Vincent'362 does not expressly teach the timing between the application of the photosensitive agents and the irradiation as within 15 minutes or 5 minutes of administration step.

Gonschlor et al. teaches the use of photofrin, also known as profimer sodium, and irradiation in reducing intimal hyperplasia (See abstract). Gonschlor et al. teaches that radiation source was employed immediately after the photosensitizing agent (See page 759, col. 1, Laser light application). Gonschlor et al. teaches that the injury was followed by the application of the photosensitizer and light source (See page 749, col. 1, first paragraph).

Harrison teaches that a stent can be used with angioplasty in order to prevent the abrupt closure of the blood vessel, which helps to maintain the blood flow and prevent further myocardial infarction (see page 986, col. 2, Second paragraph, last five lines).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ sodium profimer and irridiation together to treat and reduce IH or restenosis associated with angioplasty, where the angioplasty procedure may be involved with the use of a stent.

One of ordinary skill in the art would have been motivated to employ sodium profimer and irridiation together to treat and reduce IH or restenosis associated with angioplasty, where the angioplasty procedure may be involved with the use of a stent. According to three different studies disclosed in Vincent'362, sodium profimer is shown to be effective, when using with irradiaton, to treat or reduce IH in human stenosis cells, or in animal models. It is also known in the art that the timing of applying irradiation as immediately following the application of sodium profimer. Therefore, applying the irradiation source as recited herein would be reasonably expected to be effective in treating or reducing IH. Furthermore, it is known that stent is commonly used with angioplasty procedure in order to prevent abrupt collapse of blood vessel and at the same time maintaining blood flow to prevent myocardial infarction. Therefore, the method of employing sodium profimer to reduce or treat IH associated with angioplasty, regardless of the employment of stent or not, would be reasonably expected to be effective, absent evidence to the contrary.

Response to Arguments

Applicant's arguments with respect to claims 1-10 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
Patent Examiner
Art Unit 1617
May 2, 2003